REMARKS

Status of the Claims

Claims 2, 4-10, 24-43, 49-60, 63-66, 68-75 are pending. Claims 69, 71 and 73 are indicated as allowed and Claims 6 and 75 are indicated to be allowable.

Claims 2 and 4-9 have been amended to more clearly set forth that which Applicants regard to be the invention. Support for the amendments can be found in the specification including, for example, in the claims as originally filed.

Priority

The Office Action has denied Applicants' claim for domestic priority under 35 U.S.C. § 119(e) to U.S. Provisional Application No. 60/114,495 ('495), filed December 31, 1998, and to U.S. Provisional Application No. 60/152,195 ('195), filed September 1, 1999.

Applicants note that SEQ ID NO:3 and SEQ ID NO:4 of the present application are disclosed in Figures 1 and 2, respectively, of the '195 provisional application. Applicants further note that the claims of the present application are also disclosed in the claim set of the '195 provisional application. Thus, Applicants are entitled to the benefit of the September 1, 1999 filing date of the '195 provisional application.

35 U.S.C. § 112, first paragraph, Written Description and Enablement

Claims 2, 4, 7-10, 24-43, 49-60 and 63-66 have been rejected under 35 U.S.C. § 112, first paragraph, as allegedly not described or enabled by the as-filed specification. (Office Action, pages 4-18).

With regard to written description, the Office Action alleges that "[t]he specification does not define the term 'an HIV polypeptide that elicits a Gag-specific immune response'" (Office Action, page 5). The Office Action further alleges that "[t]he specification and the prior art of record does not disclose which nucleotides or amino acids are considered essential for eliciting a Gag-specific immune response" (Office Action, page 5). The Office Action also alleges that "[t]he skilled artisan cannot envision the detailed structure of a genus of a polynucleotide sequence encoding an HIV polypeptide that elicits a Gag-specific immune response, wherein the polynucleotide sequence encoding said polypeptide comprises a nucleotide sequence having at

least 90% sequence identity to the sequence presented in SEQ ID NO:3 or 4 that must exhibit the contemplated biological functions, and therefore, conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the structures and/or methods disclosed in the as filed specification" (Office Action, pages 7-8).

In the enablement rejection, the Office Action alleges that "the specification, while being enabling for making and using an expression cassette comprising the polynucleotide sequence set forth in SEQ ID NOs: 3 or 4, does not reasonably provide enablement for a polynucleotide sequence encoding an HIV polypeptide that elicits a Gag-specific immune response, wherein the polynucleotide sequence encoding said polypeptide comprises a nucleotide sequence having at least 90% sequence identity to the sequence presented in SEQ ID NO: 3 or 4" (Office Action, pages 10-11). The Office Action further alleges that "[t]he scope of the invention is very broad, encompassing a large number of polynucleotide sequences that may or may not encode an HIV gag polypeptide that may or may not have the desired activity" (Office Action, page 12). The Office Action further cites Baker et al. (2001) *Science* 294:93-96; Attwood (2000) *Science* 290:471-473; Gerhold et al. (1996) *BioEssays* 18:973-981; Russell et al. (1994) *J. Mol. Biol.* 244:332-350; Wells (1997) *J. Leuk. Biol.* 61: 545-550; Ngo (1994) *The Protein Folding Problem and Tertiary Structure Prediction*, Merz et al. (ed.) (Boston, MA: Birkhauser), pp. 433 and 492-495 in support of the position that undo experimentation would be required to practice the invention because of the "unpredictability of the relationship between sequence and function" (Office Action, page 13).

Applicants respectfully traverse the rejections for the reasons already made of record in the responses to the Office Actions of February 26, 2003, November 17, 2003, July 30, 2004, and January 25, 2005, the Declarations of Drs. Donnelly and Ulmer, and on the following grounds.

1. The Scope of the Genus

With respect to both written description and enablement, the Office has again asserted that the claims are overly broad and again presented various mathematical determinations allegedly showing the large the number of substitutions that may be made, both at the nucleotide and amino acid level (Office Action, pages 6 and 14-15).

The claims do **not** encompass any nucleotide sequence having 90% identity to the recited reference sequence because the sequence must also encode an immunogenic Gag polypeptide. In other words, the genus is not as broad as asserted by the Office. Nucleotides and/or amino acids may not be changed "at any position" in the molecule. For example, a nucleotide sequence comprising a stop codon that precludes the translation of an immunogenic Gag polypeptide does **not** fall within the scope of the claims. By contrast, a molecule that is 69% identical at the amino acid level but exhibits the requisite immunogenicity and requisite 90% percent identity at the nucleotide level is more than adequately described and enabled.

It is in fact clear "which activities of the HIV correspond to the claimed genus of polynucleotides with 90% sequence identity to the claimed SEQ ID NOs:3 and 4" (Office Action, page 6). The required activity is immunogenicity. Immunogenicity is not dependent on a particular primary or tertiary, and is readily assessed by methods known in the art and, indeed, working examples are set forth in the as-filed specification.

It is not clear what the Examiner means by "the claims are broader than the 90% limitation set forth in the claims because the polypeptide sequences embraced by the polynucleotide sequences having 90% identity to SEQ ID NO:3 and 4 can have a substitution of at least 30% of the amino acids of the polypeptide encoded by the claimed sequences..." (Office Action, page 14). A claim cannot be broader than itself and cannot include embodiments that are broader than any limitation recited in the claims. Thus, in the pending case, the claims cannot encompass sequences which are less than 90% homologous to the recited nucleotide sequence.

Furthermore, the amino acid sequence of the protein encoded by the claimed sequence in no way broadens the genus and, in fact, the amino acid sequence is not relevant to the requirements of Section 112, 1st paragraph. If the encoded polypeptide does not have immunogenic function (due to structure or any other reason), the molecule is not encompassed by the pending claims. As described in detail throughout the specification as filed, only those molecules that exhibit both the requisite percent identity and requisite immunogenic function are encompassed by the claimed genus.

Therefore, the claimed genus is not as broad as asserted by the Office and is limited by both structure (percent identity) and function (immunogenicity).

2. The Law Governing Written Description and Enablement

Any written description and/or enablement inquiry is dependent on the particular ***facts*** of the case. *Vas-Cath, Inc. v. Mahurkar*, 19 USPQ2d 1111 (Fed. Cir. 1991); *In re Wertheim*, 191 USPQ 90 (CCPA 1976). The facts that must be taken into account include the disclosure ***as a whole*** and the knowledge possessed by the skilled artisan at the time of filing, for example as established by reference to patents and publications available to the public prior to the filing date of the application. *See, e.g., In re Lukach*, 169 USPQ 795, 796 (CCPA 1971); *In re Lange*, 209 USPQ 288 (CCPA 1981). That which is not new need not be described in detail. *See, e.g., Capon v. Eshhar* 76 USPQ2d 1078 (Fed. Cir. 2005).

Thus, any section 112, first paragraph inquiry that does not completely or accurately assess the particular disclosure of the specification and determine the state of the field at the time of filing is flawed.

Throughout prosecution, the Office has failed to completely assess the as-filed disclosure. In particular, the Office has failed to consider the disclosure of the as-filed specification as a whole and the knowledge possessed by the skilled artisan at the time of filing. Instead, the Office has repeatedly ignored both the disclosure outside the Examples and Figures (including the background, summary, detailed description and original claims) and the state of the field (*e.g.*, determining percent identity and assessing immunogenicity). Consequently, the adequacy of the specification's disclosure has not been properly assessed with respect to description or enablement and the rejections under 35 U.S.C. § 112, first paragraph cannot be sustained.

When the actual disclosure and state of the art regarding Applicants' particular case are properly assessed, it is clear that the rejections under 35 U.S.C. § 112, first paragraph cannot be maintained. Six representative examples of sequences falling within the scope of the claims are provided in the specification. (SEQ ID NOs:1-4, 20 and 21). Further, these representative species are specifically recited in the pending claims, which, as acknowledged by the Office, are separately patentable.

Indeed, as repeatedly noted, the as-filed specification contains pages and pages of literal disclosure regarding that which is new (particularly novel sequences encoding immunogenic HIV Gag polypeptides, which the Office acknowledges are free of the art), as well as literal description of that which is conventional. It is clear from the specification as filed that

determining percent identity as between any given sequences was conventional. Equally conventional at the time of filing was determining whether a particular sequence encodes an immunogenic Gag polypeptide. There is literal disclosure in the as-filed of ***every*** embodiment encompassed by the claims.

Likewise, in addition to the six working examples, statements applicable to the genus as whole are provided throughout the specification, for example, on page 17 *et seq.* where it is noted how to determine sequences falling within the requisite percent identity. At the time of filing, determining sequence identity was utterly routine. The specification also provides guidance (*e.g.,* Example 1 of the specification) regarding selection and modification of native Gag HIV sequences. Substantial guidance is also given in regards to determining whether a Gag polypeptide is expressed from the claimed expression cassettes and whether this polypeptide is immunogenic, as required by the claims. (See, *e.g.,* Examples 2-7 and Section 2.1.3, particularly page 30). Thus, the specification provides ample guidance as to identification, generation, and testing of expression cassettes that can be used in the claimed invention.

In the pending case, the Office has taken into account only that which is exemplified. When properly assessed in its entirety, Applicants' disclosure literally discloses every embodiment falling within the scope of the claims including that which is new – namely sequences encoding non-wild-type HIV polypeptides that elicit an HIV Gag immune response.

Even if the specification did not describe multiple representative species as it does, it is well-settled that showing possession of the claimed subject matter does not, indeed cannot require actual reduction to practice of multiple possible nucleotide sequence falling within the scope of the claims. Rather, a demonstration that one of skill in the art would be aware an applicant was in possession of the sequences as claimed is sufficient to satisfy the requirements of Section 112, first paragraph.

Recently, the Federal Circuit reiterated that satisfaction of the highly fact-dependent written description requirement does **not** depend on the number of representative species (working examples) set forth in the as-filed specification (*see, Capon v. Esshar,* 76 USPQ2d 1078, 1085 (CA FC 2005):

> The "written description" requirement must be applied in the context of the particular invention and the state of the knowledge. The Board's rule that the

> nucleotide sequences of the chimeric genes must be fully presented, although the nucleotide sequences of the component DNA are known, is an inappropriate generalization. When the prior art includes the nucleotide information, precedent does not set a *per se* rule that the information must be determined afresh. Both parties state that a person experienced in the field of this invention would know that these known DNA segments would retain their DNA sequences when linked by known methods. Both parties explain that their invention is not discovering which DNA segments are related to the immune response, for that is in the prior art, but in the novel combination of the DNA segments to achieve a novel result.
>
> The "written description" requirement states that the patentee must describe the invention; it does not state that every invention must be described in the same way. As each field evolves, the balance also evolves between what is known and what is added by each inventive contribution.

In the instant case, the invention is sequences exhibiting 90% identity to the novel reference sequences and encoding immunogenic HIV Gag polypeptides. The evidence of record, including the disclosure, original claims, Declaratory evidence and references showing the state of the art, demonstrates that Applicants were in possession of the invention.

Satisfaction of Section 112, first paragraph is determined by evaluating what is disclosed, not what is exemplified (stated in the Office Action as "representative species"). In the case at hand, the disclosure as a whole amply demonstrates that Applicants' were in possession of and fully enable the claimed genus. To require exemplification of actual, multiple embodiments is contrary to ***all*** established precedent and the rejections cannot stand.

3. The Relevance of the PTO Materials on Written Description and Enablement

In response to the Applicants arguments regarding PTO Materials, the Examiner asserted that the Office's Guidelines on Written Description and Training Materials on Enablement "do not constitute substantive rulemaking and hence do not have the force and effect of law." (Office Action, pages 9 and 17).

Applicants invoked the Guidelines on Written Description (including the relevant Examples and case law cited therein), Training Material on Enablement as well as presentations by USPTO personnel to demonstrate, with Patent Office publications, that the Examiner was not applying the correct **legal** standards to the determination of adequacy of written description and

enablement. The proper legal standards are set forth in the record (see, also Section A.3. above) and further explained in the PTO Materials.

The Patent Office Guidelines on how to assess the adequacy of written description and Training Materials on Enablement plainly indicate that disclosure of even a single species can more than adequately describe and enable a broad genus. (Final Examiner Guidelines on Written Description, 66 Fed. Reg. 1099; Training Materials on Enablement). The PTO Materials include exemplary situations in which disclosure of a single species is sufficiently representative and/or enabling of large genera. (*See,* Examples 9 and 14 of the Written Description Guidelines and Example N of the Training Materials on Enablement). Indeed, the Examples in the Written Description Guidelines were favorably commented on by the Federal Circuit in *Enzo Biochem Inc. v. Gen-Probe Inc.,* 323 F.3d (Fed. Cir. 2002).

Thus, Applicants cited the Examples provided in these Materials in order to illustrate that satisfying Section 112, first paragraph does not require that multiple sequences be set forth and to remind the Examiners that there is a strong presumption that adequate written description and enablement of the claimed invention is present at the time of filing. *Vas-Cath, Inc. v. Mahurkar,* 19 USPQ2d 1111 (Fed. Cir. 1991); *In re Wertheim,* 191 USPQ 90 (CCPA 1976). These Materials reinforce the axioms that satisfaction of section 112, first paragraph does not require that the claims be limited in scope to particular sequences. Indeed, the courts have consistently found that macromolecule such as DNA and proteins may be properly defined by one or more of the following parameters: "structure, formula, chemical name or physical properties." *Fiers v. Revel*, 25 USPQ2d 1601 (Fed. Cir. 1993).

The PTO Materials summarize and apply the settled case law that there is nothing inherently unpatentable about claims directed to a broad genus. Rather, the test is whether the specification teaches how to make and use the claimed sequences and whether it reasonably conveys possession of the invention in view of a thorough reading of the disclosure and the knowledge possessed by the skilled artisan at the time of filing, for example as established by reference to patents and publications available to the public prior to the filing date of the application. *See, e.g., In re Lukach,* 169 USPQ 795, 796 (CCPA 1971). *In re Lange,* 209 USPQ 288 (CCPA 1981).

There is **no** requirement to that a description of particular sequences falling in within the scope of the claims be set forth in the as-filed specification. What is required is for written description is that the skilled artisan would know applicants were in possession of the claimed invention. For enablement, the specification need only teach one of skill in the art how to make and use the claimed subject matter.

Therefore, the PTO Guidelines and presentations by PTO personnel were properly provided as still further illustration that the specification more than adequately conveys that Applicants were in possession of and fully enabled the claimed subject matter at the time of filing.

4. The Skilled Artisan Can "Envision" Every Embodiment Encompassed by the Claims and "Conception" is Not Relevant to a Written Description Inquiry

Furthermore, the Office's statements that "the skilled artisan cannot envision the detailed structure of [the claimed] genus ... and, therefore, conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the structures and/or methods disclosed in the as-filed specification" are neither accurate nor germane to the instant written description inquiry (Office Action, page 7).

For the reasons of record and reiterated herein, the skilled artisan can envision the detailed structure of ***every*** single member of the claimed genus (a polynucleotide exhibiting 90% identity to the recited reference sequence). The specification describes, in detail, how Gag polypeptides are identified, for example by Western blotting, ELISA or the like and how to determine immunogenicity. (See, *e.g.*, Section 2.1.3, Examples 2 and 3). Further, sequences of various Gag-encoding polynucleotides (as well as Gag polypeptides themselves) were known at the time of filing and are described, for example, in the Background section and references cited therein. In fact, the specification clearly describes how to determine percent identity between polynucleotides or polypeptides, for example, in the text beginning on line 3 of page 17. Performing such alignments was routine and conventional at the time the application was filed. *See, also,* Ulmer Declaration and Examples 4-7 of the specification, describing evaluation of the Gag-specific humoral immune response by ELISA assays of anti-Gag antibody titers (see specification at page 76, lines 1-19) and of the Gag-specific cellular immune response by assays

of Gag-specific cytotoxic T-lymphocyte induced lysis of Gag peptide-pulsed target cells (see specification at page 76, line 21 through page 77, line 9). This convincing, factual evidence has been improperly ignored by the Office (*see, e.g., In re Alton,* 37 USPQ2d 1578, 1584 (Fed. Cir. 1996).

Moreover, the tenet of "simultaneous conception and reduction to practice" is not part of a written description (or enablement) inquiry. Rather, this is a standard applied in priority (interference) contests. Indeed, this passage of the Office Action embodies that the Office has continually applied the wrong standard for determining the adequacy of written description. *See, also,* sections 3 and 4 above. The test for determining satisfaction of the requirement of Section 112, first paragraph is not what is conceived or what sequences are literally described in the as-filed specification, but, rather, what the disclosure as a whole and available knowledge to determine whether the specification as-filed evinces possession of the claimed subject matter to the skilled artisan. The skilled artisan, having followed the teaching of the specification, would have no doubts that (1) Applicants were in possession of the claimed subject matter and that (2) Applicants' as-filed specification teaches how to make and use the claimed sequences. Therefore, the rejections under 35 U.S.C. § 112, first paragraph should be withdrawn.

5. *Eli Lilly*

The Examiner also again asserted that the arguments regarding cited case law were not found persuasive (Office Action, page 7).

However, the underlying fact-pattern (*e.g.,* disclosure) is what matters in determining written description and the claims and disclosure of the pending case are completely different than the claims and disclosure at issue in *Regents of the Univ. Calif. v. Eli Lilly.*

The pending claims are drawn to sequences having 90% identity to a particular **reference** sequence. The claims in *Eli Lilly* did not recite a reference sequence for the simple reason that **no** reference sequences were disclosed. Instead, the claims in *Lilly* were directed to any sequence encoding human insulin. In addition, there was no disclosure in *Lilly* of any cDNA sequences encoding human insulin.

In fact, unlike *Lilly,* the subject matter claimed in the present application is not a single sequence encoding a known protein. Rather, the pending claims, by their very nature, encompass

a variety of sequences having the recited structure and function. Unlike *Lilly*, Applicants' specification includes examples of sequences and these examples have the requisite degree of specificity (setting forth particular nucleotides). Accordingly, the skilled artisan is able to predict *a priori* the nucleotide sequence of each and every species encompassed by the claims and, in addition, would be aware Applicants were in possession of methods for making such sequences.

Thus, whereas Applicants' as-filed specification discloses at least six representative examples and the claims recite a reference sequences, *Lilly* fails to disclose any representative species and, accordingly, could not recite a reference sequence in the claims. The holding in *Lilly* is not that claims encompassing a genus of sequences can never be described but, rather, that the disclosure in *Lilly* fails to adequately describe the particular claims at issue. When properly evaluated, it is clear that Applicants' as-filed disclosure fully describes the claimed sequences.

6. "Essential" Nucleic Acids

The Examiner also asserts that the specification "does not disclose which nucleic acids are considered essential for eliciting ... a Gag-specific immune response" and cited Freed et al. (1998) as evidence that the role of HIV Gag proteins are numerous and complex (Office Action, pages 5 and 13).

In response Applicants first note their agreement with Freed et al. that the role of HIV Gag proteins are numerous and complex. However, Applicants are claiming Gag proteins having a particular role - immunogenicity. The assembly of viral particles, enzymatic activities and other interactions as between individual Gag proteins are **irrelevant** to the instant description inquiry. All that is required is that Applicants' specification reasonably convey that Applicants were in possession of polynucleotides that encode immunogenic HIV Gag polypeptides. For the reasons of record, this requirement is more than amply satisfied.

Moreover, it is not necessary for Applicants to identify nucleic acids or amino acids "essential" to immunogenicity. As previously noted, the correlation between polypeptide structure (primary sequence or tertiary structure) and immunogenic function is not one-to-one. *See, e.g.,* Dr. Ulmer's Declaration, ¶18). Contrary to the Office Action's assertions, production

of an immune response to an antigen is routinely practiced in the absence of knowledge of a protein's primary or tertiary structure. One of skill in the art can routinely produce antibodies that specifically bind to a protein by immunizing an appropriate host with oligopeptide fragments of that protein. It is well known in the art that it is possible to produce antibodies to almost any part of an antigen, and is not especially difficult to obtain antibodies with specificity for a particular protein. Furthermore, a cellular immune response is also routinely produced by immunization with antigen. The specification provides amply guidance for one of skill in the art to elicit an immune response (*i.e.*, humoral and/or cellular) with the recited polynucleotides encoding HIV polypeptides that elicit a Gag-specific immune response. *See*, specification, *e.g.*, at Examples 2-7 and Sections 2.1.3 and 2.3.

Because immunogenic function does not depend solely on primary or tertiary structure, the references cited by the Office do not establish unpredictability. (Office Action, page 13). In particular, Baker et al.; Attwood et al.; Gerhold et al.; Russell et al.; Wells et al. and Ngo et al., do **not** describe the effects of mutations on antigenic function and, accordingly, do not in any way establish unpredictability of the claimed invention. Again, the claimed antigenic variant polypeptides are not required to retain all the functional or biological properties of the native protein (*e.g.*, particle formation, etc.), but rather, are only required to have antigenic function. Polypeptides can tolerate multiple substitutions at various residues while still retaining antigenic function. One of skill in the art can routinely produce antigenic polypeptides, and polypeptides that are not immunogenic are not encompassed by the claims.

Given the highly fact-dependent nature of the written description and enablement inquiries, it is clear that the Office's continued insistence on recitation of "essential" residues (both polynucleotide and amino acid) is inappropriate and unnecessary in claims, such as the pending claims, where the recited function is immunogenicity – a function in which there is no one "essential" residue.

It is clear that the specification describes and enables one of skill in the art to generate an immune response to any protein without knowing the particular sequence of the protein. In particular, Applicants reiterate that the specification clearly describes that the recited polynucleotides, encoding immunogenic HIV Gag polypeptides, may produce a range of antibodies recognizing different epitopes and/or may generate CTL or other cellular immune

responses. One of skill in the art would know to make and use the claimed molecules and would have known that Applicants were in possession of molecules that elicit such immune responses by virtue of the specification's clear disclosure of particular examples and general knowledge regarding generating and measuring immune responses. It is not necessary that multiple protein-encoding sequences falling within the scope of the claim be described in order to meet the written description and/or enablement requirements.

7. Declaratory Evidence of Record Has Not Been Properly Considered

As noted in the record and above, the Declarations of Drs. Donnelly and Ulmer, previously submitted on December 18, 2002 and January 20, 2004 (respectively) further establish that the sequences having at least 90% identity to SEQ ID NO:3 or SEQ ID NO:4 are enabled and described.

Drs. Donnelly and Ulmer attest to the fact that one of skill in the art could have readily made and used the compositions and methods of the pending claims in light of the specification, together with the common general knowledge, tools and methods available in December 1999. *See,* Donnelly Declaration, ¶7 and Ulmer Declaration, ¶11).

Drs. Donnelly and Ulmer also establish that the specification also provides guidance for evaluating whether sequences having 90% identity to SEQ ID NO:3 or SEQ ID NO:4 encode HIV polypeptides that elicit a Gag-specific immune response. *See,* Donnelly Declaration, ¶8 and Ulmer Declaration, ¶12.

Moreover, Dr. Ulmer establishes that immunogenicity does is not directly correlated with either primary or tertiary structure (Ulmer Declaration, ¶18, emphasis added):

> 18. Third, the specification unambiguously and clearly describes at the time of filing, the correlation between structure of the claimed biomolecules and their immunogenic function. ... Furthermore, those of us working in this field knew, at the time of filing, that **any given antigen can tolerate a number of amino acid substitutions while still retaining its immunogenic function. In other words, a particular amino acid sequence is not required in order to elicit a *Gag*-specific immune response. Rather, one would expect that a multitude of *Gag* polypeptides, having different amino acid sequences, would function to generate specific an immune response in a subject.** Thus, it would have been clear to the skilled worker that the specification describes the correlation between the structure and function set forth in the claims.

Thus, using specific facts, Drs. Donnelly and Ulmer conclude that the as-filed specification describes and enables the claimed subject matter. This convincing, factual evidence has been improperly dismissed by the Office (*see, e.g., In re Alton,* 37 USPQ2d 1578, 1584 (Fed. Cir. 1996).

8. Definition of the term "Gag-specific" immune response

The Office Action also alleges that the specification does not define the term "Gag-specific immune response." Applicants respectfully traverse and again direct the Examiner's attention to page 14, lines 14-16, which states (emphasis added):

> An "immunogenic composition" is a composition that comprises an antigenic molecule where administration of the composition to a subject results in the development in the subject of a humoral and/or cellular immune response to the antigenic molecule of interest.

Thus, the skilled artisan would clearly recognize, from the teachings of the specification and from the generally understanding of the term, what is meant by a Gag-specific immune response.

Nonetheless, in a sincere effort to advance prosecution, the offending recitation has been removed from the claims. Accordingly, this ground of rejection have been obviated.

In sum, the Examiner has failed to make out a *prima facie* case of nonenablement or lack of description. The evidence of record is clear -- every single nucleotide species exhibiting 90% identity to the **claimed** reference sequence can be determined *a priori* and, accordingly, is described and enabled by the specification as filed. The functional **recitations** in all the claims, namely that the protein encoded be an immunogenic HIV *Gag* protein, make the Office's assertions regarding (1) the breadth of the claims; (2) the amount of identity at the amino acid level and (3) the alleged lack of structure-function correlation erroneous and/or irrelevant.

Thus, for the reasons of record and above, the specification describes and enables the claimed subject matter. Reconsideration and withdrawal of the rejections under 35 U.S.C. § 112, first paragraph, are respectfully requested.

Rejections Under 35 U.S.C. § 102(f)

Claims 2, 4, 5, 24, 25, 41, 68, and 74 remain rejected under 35 U.S.C. § 102(f) on the grounds that the applicant allegedly did not invent the claimed subject matter. As evidence in support of this rejection, the Examiner refers to co-pending U.S. Application No. 09/967,464 and to U.S. Publication No. 2003/0138453. Applicants note that U.S. Application No. 09/967,464 was published by the Patent Office as U.S. Publication No. 2003/0138453 and, as such, U.S. Publication No. 2003/0138453 and U.S. Application No. 09/967,464 refer to the same (identical) patent application.

The Office Action alleges that claim 72 of co-pending application 09/967,464 ('464) and U.S. Patent Publication No. 2003/0138453 ('453) recite a microparticle comprising a vector comprising a heterologous nucleic acid sequence that encodes an HIV Gag polypeptide having a sequence having at least 90% identity to nucleotides 844-903 of SEQ ID NO: 63 (100% identity with SEQ ID NO: 3 of the instant invention), nucleotides 82-1512 of SEQ ID NO: 68 (and 99% identity to SEQ ID NO: 4 of the instant invention). The Office Action further alleges that although the claims do not specifically recite a promoter operably linked to the heterologous nucleic acid, a promoter would be required in the vector to express the heterologous nucleic acid because a promoter is required for the heterologous nucleic acid to be expressed in a cell and the language of the instant claims does not exclude additional elements (Office Action, pages 18-21). Applicants respectfully traverse the rejections.

As is well known, a named inventor must contribute to the conception of the claimed invention. The '464 application includes claims directed to subject matter which is not claimed in the present application. In particular, Claims 2, 4, 5, 24, 25, 41, 68, and 74 of the present application relate to particular expression cassettes and recombinant expression systems and generic compositions comprising the expression cassettes. As defined in the present application, the term "expression cassette" refers to a nucleic acid assembly which is capable of directing the expression of a sequence or gene of interest (see, e.g., page 24, lines 22-26 of the present application). In contrast, the claims of the '464 application relate to microparticles with adsorbent surfaces wherein nucleic acid molecules are adsorbed thereto, methods of making such microparticles and uses for the microparticles. Importantly, as defined in the '464 application,

the term "microparticles" refers to polymer microparticles and submicrom emulsion compositions, and does not denote nucleic acid expression cassettes. Thus, given that the present application and the '464 application claim different subject matter, it is reasonable that different inventors are specified in each of the applications as each named inventor would have contributed to different aspects of the conception of the claimed inventions.

At pages 19 and 21 of the Office Action, the Office indicated that Applicants' argument is not persuasive because "the claims from '464 and the instant claims ... both comprise a polynucleotide encoding a HIV polypeptide wherein the polynucleotide encodes an HIV polypeptide wherein the polynucleotide ... comprises a nucleotide sequence having at least 90% sequence identity to the sequence presented as Figure 1 or Figure 2 of the instant application" and the "language of the instant claims (expression cassette comprising) do[es] not exclude the additional elements set forth in the claims from '464". Respectfully, Applicants do not understand this argument as it would appear to suggest that a countless number of unknown individuals could be inventors since a countless number of unknown elements invented by others could be added in the claims of the subject application, including the additional elements set forth in the claims from the '464 application. Clarification is respectfully requested.

The Examiner is reminded that a rejection under 35 U.S.C. §102(f) is appropriate "[w]here it can be shown that an applicant 'derived' an invention from another ..." (*See Ex parte Kusko*, 215 USPQ 972, 974 (Bd. App. 1981)). Here, the Examiner has provided no such showing. Rather, the mere fact that certain claims of the '464 application recite the use of components that are also recited in certain claims of the present application is insufficient to raise a presumption that justifies a rejection under 35 U.S.C. §102(f):

> "The mere fact that a claim recites the use of various components, each of which can be argumentatively assumed to be old, does not provide a proper basis for a rejection under 35 U.S.C. 102(f)." ... Derivation requires complete conception by another and communication of that conception by means to the party charged with derivation prior to any date on which it can be shown that the one charged with derivation possessed knowledge of the invention. ... "Communication of a complete conception must be sufficient to enable one of ordinary skill in the art to construct and successfully operate the invention." ...

(*See* MPEP § 2137, citations omitted.) Indeed, as discussed above, Claims 2, 4, 5, 24, 25, 41, 68, and 74 of the present application are fully supported by provisional application 60/152,195 ('195), which has a filing date of September 1, 1999. The '464 application cited above was filed **after** the present application; indeed, the earliest priority date of the '464 application (September 28, 2000) is more than one year after the filing date of Applicants' '195 provisional application. Thus, Applicants submit that the Office has not met its burden to establish that the present inventors derived their claimed invention from others.

Moreover, the inventors in the present application signed a declaration under 37 CFR §1.63 filed February 29, 2000, stating that they believe they are the first and original inventors of the subject matter claimed in the present application. This declaration creates a presumption that the parties signing the declaration are in fact the inventors (*See* MPEP § 2137.01(I), citing *Driscoll v. Cebalo*, 5 USPQ2d 1477, 1481 (Bd. Pat. Inter. App. 1982)).

In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of the rejections under 35 U.S.C. § 102(f).

Provisional Rejections Under Nonstatutory-Type Double Patenting

The Office has maintained several provisional rejections under the judicially created doctrine of obviousness-type double patenting. These provisional rejections are as follows:

A) Claims 2, 4, 5, 24, 25, 41-43, 68 and 74 remain provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 26, 28, 31-50 and 72 of copending U.S. Application No. 09/967,464 ('464) or of U.S. Publication No. 2003/0138453.

B) Claims 2, 24 and 25 remain provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over Claims 26, 28, 31-50 and 72 of the '464 application or of U.S. Publication No. 2003/0138453 in view of Tartaglia et al. (U.S. Patent No. 5,990,091) and Corbin et al. (U.S. Patent No. 6,489,542).

C) Claims 2 and 24-26 remain provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over Claims 26, 28, 31-50 and 72 of the '464 application or of U.S. Publication 2003/0138453 in view of Tartaglia et al.

(U.S. Patent No. 5,990,091) and Corbin et al. (U.S. Patent No. 6,489,542) and either Sikic et al. (U.S. Patent No. 5,830,697) or Dubensky et al. (U.S. Patent No. 6,391,632).

D) Claims 2 and 27-40 remain provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 26, 28, 31-50 and 72 of the '464 application or of U.S. Publication No. 2003/0138453 in view of ATCC catalog of cell lines and hybridomas (7th edition, Maryland, 1992, pages 70, 79, 148, 150, 158, 164, 194, 299, 308 and 456); Helting et al. (U.S. Patent No. 5,470,720); and Adams et al. (IJ-1).

E) Claims 68 and 70 remain provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 26, 28, 31-50 and 72 of the '464 application or of U.S. Publication No. 2003/0138453 in view of Rovinski et al. (BS-1).

F) Claims 68 and 72 remain provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 26, 28, 31-50 and 72 of the '464 application or of U.S. Publication No. 2003/0138453 in view of Rovinski et al. (BE-1).

As indicated above, the '464 application published as U.S. Publication No. 2003/0138453 and, as such, the '464 application and U.S. Publication No. 2003/0138453 refer to the same patent application.

As each of these rejections are *provisional* rejections, Applicants request that they be held in abeyance until there is an indication of allowable subject matter in either the present application or in the '464 application.

Moreover, as discussed above, the present application was filed on December 30, 1999, with priority to September 1, 1999. In contrast, the '464 application was filed on September 28, 2001, claiming priority to two U.S. provisional application, the earliest of which was filed September 28, 2000. Thus, the present application is the earlier filed application. MPEP § 804 provides that if a provisional nonstatutory obviousness-type double patenting rejection is the only rejection remaining in the earlier filed of the two pending applications, the examiner should withdraw that rejection and permit the earlier-filed application to issue as a patent without a terminal disclaimer (*See* MPEP § 804(I)(B)(1)).

Claims 2, 4, 5, 24-26, 41-43, 68 and 74 remain rejected on the grounds that they are directed to an invention not patentably distinct from claims of the '464 application and U.S. Publication No. 2003/0138453 for the reasons set forth in the provisional double patenting rejections. The Office alleges that the '464 application would form the basis for a rejection of the noted claims under 35 U.S.C. § 103(a) if the commonly assigned case qualifies as prior art under 35 U.S.C. § 102(f) or (g) and the conflicting inventions were not commonly owned at the time the invention in the present application was made.

As discussed above, the claims of present application and the claims of the '464 application relate to different subject matter. Moreover, as noted by the Office, the present application and the '464 application are assigned to Chiron Corporation. Thus, the claimed inventions in the present application and the '464 application were commonly owned by Chiron Corporation at the time they were made.

CONCLUSION

In light of the above amendments and remarks, Applicants submit that the present application is in condition for allowance. If the Examiner contemplates other action, or if a telephone conference would expedite allowance of the claims, Applicants invite the Examiner to contact the undersigned.

The Commissioner is hereby authorized to charge any fees and credit any overpayment of fees which may be required under 37 C.F.R. §1.16, §1.17, or §1.21, to Deposit Account No. 18-1648.

Please direct all further written communications regarding this application to:

Helen Lee
NOVARTIS VACCINES AND DIAGNOSTICS
Intellectual Property - R440
P. O. Box 8097
Emeryville, CA 94662-8097
Tel: (510) 923-2192
Fax: (510) 655-3542

Respectfully submitted,

Date: May 16, 2006

By: Dahna Pasternak
Dahna S. Pasternak
Registration No. 41,411

NOVARTIS VACCINES AND DIAGNOSTICS
Intellectual Property - R440
P. O. Box 8097
Emeryville, CA 94662-8097